

## II. REMARKS

Claims 1-20 are presently pending in the application. Claims 1-4 and 7-19 have been withdrawn from consideration and examined claims 5, 6 and 20 stand rejected under 35 U.S.C. §§ 112 and 102. The examined claims have been amended herein in a sincere effort to expedite prosecution. Support of the recitation of "dimerizing peptide" and "8 to 25 amino acids in length" can be found throughout the application as filed, for example on page 11, lines 15-22. Claim 5 has also been amended to clarify that the complexes are made up of multiple zinc finger proteins which in turn are made up of a plurality of zinc finger components, as described for example on page 11, lines 12-14 stating that dimerizing "peptides are useful for mediating association of complexes of multiple zinc finger proteins ..."; and page 14, lines 12-15. Entry of the foregoing amendments and consideration of the following remarks is respectfully requested.

### **Drawings**

The objection to the drawings has been maintained. In this regard, the Office repeatedly states that the original specification contained only two Figures and that the substitute specification somehow added drawings. (Final Office Action, page 2). However, contrary to the Examiner's assertion there is a perfect correspondence between the drawings in the as-filed specification and those presented in the substitute specification. Indeed, the as-filed specification contained a total of 9 drawings -- 2 Figures described in the "Brief Description of the Figures;" 4 drawings embedded in Example 1 (labeled as Figure 1-4 in Example 1 of the as-filed application); and 3 drawings embedded in Example 2 (labeled as Figures 1-3 in Example 2 of the as-filed application). As detailed in the preliminary amendment filed with the substitute specification, the labels of the Figures embedded within Examples 1 and 2 of the as-filed specification were corrected and the Brief Description of the Drawings amended as follows:

Reference No. in as-filed Spec	Reference No. in substitute Spec
Figure 1 in Brief Description	Figure 1 in Brief Description
Figure 2 in Brief Description	Figure 2 in Brief Description
Figure 1, panels A-C of Example 1	Figure 3, panels A-C in Brief Description
Figure 2, panels A-B of Example 1	Figure 4, panels A-B in Brief Description
Figure 3 of Example 1	Figure 5 in Brief Description
Figure 4 of Example 1	Figure 6 in Brief Description
Figure 1 of Example 2	Figure 8 in Brief Description
Figure 2 of Example 2	Figure 9 in Brief Description
Figure 3 of Example 2	Figure 7 in Brief Description

Thus, the as filed and substitute specification contain the same number of drawings and the substance and description of these drawings is identical to those contained in the as-filed specification. Accordingly, Applicants request withdrawal of this objection.

### Specification

The objection to the specification is also maintained. In particular, the manuscript-type material in Examples 1 and 2 is alleged to be confusing. In their previous amendment, Applicants eliminated the duplicative occurrences of the heading "abstract." Nonetheless, the Examiner asserts:

...elimination of the heading "abstract" does not remove the confusion as to the presence of said abstract in the Examples. In patent applications, working examples provided in the specification should admit an illustration of the invention and should not contain a disclosure of the general background of the prior art or an abstract. Thus, the incorporation of the entire manuscripts in the Examples is confusing. Cf. with the provisional application of 60/148,422, filed on 8/11/99, which did not include applicants' own work, i.e., the entire manuscripts. (Office Action, page 4).

Applicants note that there is no requirement prohibiting an applicant from discussing references or other background information in the Example section. Rather, an applicant is free to include any information they deem appropriate in the detailed description of their specification. (See, also, Office Action, mailed September 25, 2002, where the Office correctly noted, "the Examples need not contain a disclosure of the general background...") Indeed, manuscripts are often incorporated verbatim into patent applications. Furthermore, there is no requirement that a utility application be identical to the provisional application from which priority is claimed. Nonetheless, to help clarify for the Examiner, Applicants would be willing to delete certain material from the Examples.

### 35 U.S.C. § 112, first paragraph, written description

Claims 5, 6 and 20 stand rejected as allegedly not described in the specification as filed in such a way as to reasonably convey to the skilled artisan that applicants were in possession of the claimed invention. (Final Office Action, pages 5-6). In support of this rejection, the Office states:

The as-filed specification does not contain a description of a zinc finger complex comprising more than two fusion proteins linked via the non-naturally occurring peptide sequences. There is no description in the specification as to the maximum limit of the term "more" than two fusion proteins. More importantly, there is no description as to whether the linking of the two linkers result in a stable fusion protein complex containing more than two zinc finger fusions. This is confusing since the Examples do not describe any linking of non-naturally occurring peptide linkers to fuse more than two zinc finger proteins of similar sequences. Furthermore,

the as-filed specification does not describe a zinc finger protein having the same sequence. (Office Action, pages 5-6).

To the extent that the written description rejection is not obviated by the foregoing amendments, Applicants traverse the rejection and supporting remarks.

The fundamental factual inquiry in written description is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. *See, e.g., Vas-Cath, Inc.*, 935 F.2d at 1563-64, 19 USPQ2d at 1117. Determining whether the written description requirement is satisfied is a question of fact and the burden is on the Examiner to provide evidence as to why a skilled artisan would not have recognized that the applicant was in possession of claimed invention at the time of filing.

*Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim*, 191 USPQ 90 (CCPA 1976). It is not necessary that the application describe the claimed invention *in ipsius verba*. Rather, all that is required is that the specification reasonably conveys possession of the invention. *See, e.g., In re Lukach*, 169 USPQ 795, 796 (CCPA 1971). Finally, determining whether the written description requirement is satisfied requires reading the disclosure in light of the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lange*, 209 USPQ 288 (CCPA 1981).

Because any written description inquiry must begin with claim construction, it is important to note at the outset of this discussion that the claims clearly recite that the complexes include multiple zinc finger proteins linked via dimerizing peptides of 8-25 amino acids in length. Furthermore, each zinc finger protein contains a plurality of zinc finger components, i.e., is a multi-finger (polydactyl) zinc finger protein. Thus, the claims do not, as asserted by the Office, encompass any and all fusion proteins.

The specification as filed fully describes the claimed subject matter. The specification describes, in detail, how multiple polydactyl zinc finger proteins are linked using dimerizing peptides of about 8-25 amino acids in length. (See, e.g., page 11, lines 12-14; page 11, lines 20-22 and Examples 1 and 2). Further, the specification clearly describes how the complexes can include two or more of such zinc finger proteins and how the proteins can be the same or different:

Dimerizing peptides selected by phage display are useful for mediating multimerization of zinc finger proteins or other types of protein. A typical application of such peptides is to mediate association of two different zinc finger proteins that have proximate target segments within a target sequence. (See, page 12, lines 20-23)...

Different zinc finger proteins can be used preassociated or can be used separately in which case they associate *in situ*. Often zinc finger proteins linked to dimerizing peptides of the invention remain dissociated in solution, and dimerized

only on binding to DNA. Such is advantageous in promoting dimerization between two different zinc finger proteins linked to the dimerizing peptides relative to homodimerization of the two copies of the same zinc finger protein. For example, if a target sequence contains adjacent sites for two different zinc finger proteins, both zinc finger proteins can bind simultaneously to the target sequence, and then dimerize with each other mediated by the linked dimerizing peptide. By contrast, two copies of the same zinc finger cannot usually bind adjacent to each other on the same target sequence (unless by coincidence the target contains an inverted repeat of the target site for that zinc finger). (See, page 13, lines 22-34).

Thus, there is clear description in the specification as filed regarding all the claimed elements. In view of disclosure of the specification and state of the art, it would have been plain to the skilled artisan that Applicants were in possession of the claimed subject matter at the time the specification was filed.

### **35 U.S.C. § 112, second paragraph**

Claims 5 and 6 are rejected as allegedly indefinite. (Office Action, pages 6-7). In particular, the term "two or more" is alleged to be unclear as it relates to fusion peptides. (Office Action, page 6). In addition, the metes and bounds of the term "nonnaturally occurring peptides" are alleged to be not clearly set forth. (Office Action, page 7).

Although Applicants submit that the claims were sufficiently clear and definite as filed, claims 5 and 6 have been amended herein to remove (1) the terms "two or more fusion proteins" and (2) to clarify the structure and function of the non-naturally occurring dimerizing peptides.

In view of the foregoing amendments and remarks, Applicants request withdrawal of the rejections based on 35 U.S.C. 112, second paragraph.

### **35 U.S.C. 102**

Claim 5 stands rejected as allegedly anticipated by Kim et al. (PNAS 3/98) and claims 5, 6, and 20 stand rejected as allegedly anticipated by Pavletich et al. (Science 1991). (Office Action, pages 7-9).

Because neither Kim nor Pavletich teach or suggest the claimed molecules, Applicants traverse the rejection.

As noted above, the pending claims are directed to complexes containing multiple zinc finger proteins linked via at least two dimerizing peptides (one with each zinc finger protein). Furthermore, each zinc finger protein includes multiple zinc finger components. In contrast, Kim and Pavletich do not describe either (1) linkage via dimerizing peptides or (2) linkage of zinc finger proteins to each other. Rather, these references each disclose "linkage" of individual zinc finger components within a single zinc finger protein using one (non-dimerizing) linker between the components of the larger

protein. Thus, Kim and Pavletich contain absolutely no disclosure regarding linking a plurality of multi-fingered zinc finger proteins together where each ZFP contains its own dimerizing peptide linker. Accordingly, Kim and Pavletich fail to describe, demonstrate or suggest the molecules as claimed, Applicants submit that withdrawal of this rejection is in order.

**CONCLUSION**

Applicants believe that the claimed subject matter is now in condition for allowance and early notification to that effect is respectfully requested. If any issues remain to be addressed, the Examiner is encouraged to telephone the undersigned.

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Respectfully submitted,

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